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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,761	06/01/2001	John T. Mulligan	340078.401	9920

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	13

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/872,761	MULLIGAN ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) 2 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-3 and 5-10 and species DHPLC in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Sequence Rules Compliance

2. The original filed sequencing listing has complied With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Objections

3. Claim 1 is objected to because of the following informalities: Note that " HPLC" and "DHPLC" are abbreviations. They can only be used after each phrase appears once.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6, 7, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The term " larger" in claims 6 and 10 is a relative term which renders the claim indefinite. The term "larger" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

7. Claim 7 recites the limitation " the side product separated" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no side product in claims 1 and 3.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3, 5, 6, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huber *et al.,* (Anal. Chem., 68, 2959-2965, 1996) in view of Tang *et al.,* (US Patent No. 5,668,268, published on September 16, 1997) and Agabian *et al.,* (US Patent No. 5,770,714, published on June 23, 1998).

Regarding claims 1 and 3, Huber *et al.,* teach the detection of partial denaturation in AT-rich DNA fragments by ion-pair reversed-phase chromatography. In the assay, Hae III digests ranging in length from 46 to 910 bp from double stranded pRB322 DNA were separated by a HPLC system at different temperatures. Small digested fragments less than 120 bp were completely denatured between 53.6 and 63.5 ^{0}C. At 70 ^{0}C, all digested fragments were denatured and eluted from the column as two peaks. A shape peak comprised a fragment of 51 bp and a broad peaks comprised all other fragments in length from 46 to 910 bp (see abstract in page 2659, page 2960, and Figure 1). Note that: (1) two peaks in HPLC profiles at 70 ^{0}C were considered as two populations of double stranded oligonucleotides as recited in claim 1; and (2) HPLC performed between 53.6 and 70 was considered as DHPLC since the separation was carried out under denaturing conditions.

Huber *et al.,* do not disclose to separate synthetic double-stranded oligonucleotides into two populations of which one population is enriched for synthetic failures and the other population is depleted of synthetic failures as recited in claim 1.

Tang *et al.,* showed that n mer oligonucleotide was contaminated with n-1 contaminant during the process of chemical synthesis (see column 2, second paragraph).

Regarding claims 5, 6, and 8-10, Agabian *et al.,* teach that double stranded DNA fragments can be synthesized by annealing and ligating a plurality of chemically synthesized single-stranded fragments (see column 4, second paragraph). A double stranded DNA fragment was considered as a larger DNA molecule comprising one or more fragments as recited in claims 6 and 10 since 5' part of the double stranded DNA fragment could be considered as the first fragment while 3' part of the double stranded DNA fragment could be considered as the second fragment.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have separated synthetic double-stranded oligonucleotides into two populations of which one population was enriched for synthetic failures and the other population was depleted of synthetic failures under denaturing conditions using DHPLC in view of the prior art of Huber *et al.,* Tang *et al.,* and Agabian *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Huber *et al.,* because the using a well known double stranded DNA separation method for separating different double stranded nucleic acids (the replacement of digested double stranded DNA with synthetic double stranded oligonucleotide for the separation) would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

10. No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
November 13, 2002

ETHAN C. WHISENANT
PRIMARY EXAMINER